

Nonetheless, Applicant hereby submits the declaration of Dr. Pamela Hilpert, entitled "Fourth Declaration of Pamela Hilpert" (hereinafter "Hilpert Declaration" or "her declaration") which further substantiates Applicant's position that the specification complies with the written description requirement as to these claims. The declaration provides a factual statement as to what is disclosed and how such disclosure reasonably conveys to one skilled in the art that Applicant was in possession of the claimed invention.

As set forth in her declaration, Dr. Hilpert has extensive experience with ultrasound contrast agents. More importantly, Dr. Hilpert's experience shows that she is very knowledgeable concerning what those skilled in the art were aware of in the 1991 time frame, since her review article on the subject was published at that time.

Having reviewed the present specification, and in light of her experience and knowledge regarding the state of the art in the relevant time frame, Dr. Hilpert concludes that one skilled in the art in that time frame would have readily understood that a contrast enhancing agent of microbubbles of perfluoropropane was part of the invention described and claimed. Indeed, the Examiner admits that the specification teaches the use of perfluoropropane. (See Office Action of September 22, 1998, page 3.) Dr. Hilpert likewise concludes that similar agents containing perfluorobutane or perfluoropropane, which are covered in non-elected claims 15-29, would also be

readily understood as part of the invention.

However, Dr. Hilpert also concludes that one skilled in the art in that time frame likewise would have readily understood that the contemplated invention included such agents together with aqueous solutions or suspensions of protein, liposomes, microspheres, or of crystals in a saccharide diluent. That is, the claimed combinations of claims 31-34 and newly added claim 35 were indeed part of the disclosed invention and would be recognized as such by one skilled in the art.

In reaching this conclusion, Dr. Hilpert points specifically to guidance in the specification which would convey to the skilled artisan that the Applicant was indeed in possession of the claimed invention. Dr. Hilpert points in particular to pages 20-21 of the section entitled "Brief Description of the Invention." (Hilpert Declaration, paragraph 6(1).) In this section, as Dr. Hilpert notes, the Applicant describes the invention as a method to select particular gases, and that the selected gases "can be used to produce the contrast enhancing media that is also the subject matter of the invention." Once the gas selection is made, this section, again as noted by Dr. Hilpert, makes further reference to using "existing techniques" to produce "improved contrast-enhancing media."

According to Dr. Hilpert, these statements would be understood by one skilled in the art as conveying that Applicant considered his invention to include

both (1) selecting particular gases based on the disclosed method, and (2) incorporating the gases into a contrast-enhancing agent using any technique otherwise then known. (Hilpert Declaration, paragraph 6(1).)

As Dr. Hilpert further points out, this discussion of "existing techniques" conveys to one skilled in the art, at the very least, that the Applicant contemplated the use of those existing techniques explicitly disclosed in the specification in combination with the selected gases. (Hilpert Declaration, paragraph 6(4).) These techniques include the uses of human protein, liposomes, or microspheres, or of crystals suspended in a saccharide diluent. (see pages 6-20.) Therefore, at the very least the specification conveys the selection of the claimed gas perfluoropropane in combination with the above disclosed existing techniques, as presently claimed in claims 31-35.

In further support of the above, it should also be noted that the use of aqueous solutions or suspensions of protein or microspheres, or of suspended crystals was so well known in the art at the time as to be discussed in Dr. Hilpert's 1991 review paper of ultrasound contrast agents (see Hilpert Declaration, paragraphs 6(6)-(11) and Exhibit 1 to Hilpert Declaration). The fact that these techniques were in accepted use in ultrasound art further strengthens Applicant's position that the claimed combinations would be understood to be part of the

invention.

On the basis of the foregoing and Applicant's prior response, Applicant submits that the disclosure meets the legal standard of reasonably conveying to one skilled in the art that Applicant was in possession of the claimed invention. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, with respect to claims 30-35 is again respectfully requested.

Applicant further notes that in Applicant's previous response, at page 14, Bichon et al. (U.S. Patent 5,711, 933) was referenced as being concurrently submitted therewith. In fact, this reference was inadvertently omitted from the information disclosure statement that accompanied the previous response. Applicant is submitting an additional information disclosure statement herewith that contains a copy of Bichon et al. and apologizes for the oversight.

Respectfully submitted,
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